15/Declaration
1.132

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ATTY.'S DOCKET: MATSUDA13

In re Application of:

Katsuya MATSUDA, et al.

Serial No.: 09/807,190

Filed: April 10, 2001

For: POLYMER COMBINING WITH PHOSPHORIC ACID AND...

Art Unit: 1615

Examiner: A.E. PULLIAM

Confirmation No. 4190

Washington D.C.

April 4, 2003

SUBMISSION OF EXECUTED DECLARATION

Honorable Commissioner for Patents
Washington, D.C. 20231

Supplemental to the amendment filed March 21, 2003, please enter the executed declaration submitted herewith.

Respectfully submitted,

BROWDY AND NEIMARK
Attorneys for Applicant(s)

By _____
Anne M. Kornbau
Reg. No. 25,884

624 Ninth Street, N.W., Suite 300
Washington, D.C. 20001-5303
Telephone: (202)628-5197
Facsimile: (202)737-3528

AMK:nmp

C:\BN\Y\YUAS\Matsuda 13\PTO\apr 4 03 dec submission.doc

CERTIFICATE OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the Patent and Trademark Office to **Examiner A.E. PULLIAM** at **703-746-4997**

_____
NeNola Permenter

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: (Art Unit: 1615

Katsuya MATSUDA et al (Examiner: P. KULKOSKY

Appln. No.: 09/807,190 (Confirmation No. 4190

Filed: April 10, 2000 (Washington D.C.

For: POLYMER COMBINING WITH PHOSPHORIC ACID AND PREPARATION CONTAINING THE SAME (March, 2003

DECLARATION UNDER CFR 1.132

Honorable Commissioner for Patents and Trademarks,

Washington, D.C. 20231

Sir:

I, Katsuya MATSUDA, declare and state that I am one of the applicants of the above-identified patent application.

I declare that I graduated in March 1981 from the Faculty of Technology, Keio University, Yokohama, Japan and that I received a bachelor degree in Engineering from the same University.

I declare further that I have been employed by Chugai Seiyaku Kabushiki Kaisha, the assignee of the present application, since 1981 and that I have been engaged, as a researcher, in research into solid dosage formulations.

I declare furth r that I am a Senior Researcher at Production Technology Laboratory of the Assignee.

I declare further that I have read all of the Official Actions in the above-identified application, and have read and am familiar with each of the references cited in the Official Action by the Examiner.

I declare further that the following test was conducted at my direction or under my supervision, and that the test results are true and correct to the best of my knowledge.

1. The relation between the method for preparation of phosphate-binding polymers and the true specific gravity of the polymers.

According to the method described in "Preparation 1" or "Preparation 2" on page 12 of the specification of the present application, phosphate-binding polymers were prepared by crosslinking polyallylamine with epichlorohydrin in a mixed medium of water/acetonitrile (ca. 50:50 w/w) (Preparation 1) or in water (Preparation 2).

The conditions for conducting the method for preparation of phosphate-binding polymers "a", "d" and "i" are summarized in Table I below.

Table I

Lot	a	d	i
Production Scale	30.9(kg)	63(kg)	59.7(kg)
Polyallylamine	1	1	1
Water	4	4	4
Sodium hydroxide	0.28	0.3	0.306
Acetonitrile	0	4.8	4.8
Epichlorohydrin	0.093	0.094	0.094

The resulting polymer was dried and ground into particles of water-containing phosphate-binding polymers and the true specific gravity of the polymers was measured using an apparatus for measuring true specific gravity (Acupick Model 1330, Shimazu Seisakusho K.K. Japan) by means of Helium gas substitution method.

The results are shown in the following Table II.

Table II

Solvent Used	Lot	True Specific Gravity(g/ml)	Remarks
Water	a*	1.2530	* The data shown in Table 1 on page 13 of the present application. (Samples prepared by the method of Holmes)
	b*	1.2527	
	c	1.2549	
Water/Acetonitril	d**	1.2094	**The data shown in Table 1 on page 13 of the present application
	e**	1.2107	
	f**	1.2108	
	g	1.2062	
	h	1.2174	
	i	1.2084	
	j	1.2049	
	k	1.2044	
	l	1.2087	
	m	1.2089	

As is clear from th data in Table II, a polymer prepared by the method of "Preparation 2" in the present application or by the method of Holmes always had a true specific gravity of more than 1.25. On the other hand, a polymer prepared by the method of "Preparation 1" had a true specific gravity of 1.20 to 1.22.

2. Hardness and Maximum Weight Loss of uncoated tablets obtained from polymers prepared by "Preparation 1" or "Preparation 2".

(a) A polymer is compressed under a static pressure of 1750 kg into tablets of 10 mmϕ each weighing 300 mg as shown in Example 1 of the present application. The tablets obtained from a polymer having a true specific gravity of 1.253 and prepared by Holmes (or Preparation 2) showed 3.6 KP and 5.6 KP. Incidentally, a compression pressure of around 2,000 kg for preparing tablets is almost the acceptable upper limit to a tableting machine. If the machine is continuously used at a compression pressure over the limit, it will cause fatigue failure of punches of the tableting machine.

On the other hand, the polymers of the present invention having a true specific gravity of from 1.209, 1.211 and 1.211, respectively provide tablets having a hardness of 23.9 KP, 24.3 KP and 15.5 KP, respectively.

Please refer to Table 1 on page 13 of the specification of the present application.

(b) According to the similar method of Example 3, tablets containing the polymer were prepared with a tableting machine at a compression pressure of 2000 kg or 900 kg. The polymer had a true specific gravity of 1.21 and a water content of 5.1%. Tablets prepared had a weight of 290 mg/tablet, a diameter of 9.5 mmϕ and contained 250 mg of the polymer per tablet on a dry basis.

The thus prepared tablets were subjected to a test for measuring a maximum weight loss according to The United States Pharmacopeia (USP) 24, The National Formulary (NF) 19, No. 1216-Tablet Friability. The test were conducted at 25 rpm for 30 minutes.

The test results are shown in the following Table III. The results are an average of 20 tablets.

Table III

Lot	Compression Pressure (kg)	Hardness (KP)	Weight Loss (%)
F-1	2,000	16.7	0.85
F-1B	900	5.0	4.23

As is clear from the test results in Table III, the tablet having a hardness of 5 KP showed a weight loss of 4.23% which is not deemed to be desirable for coating process. While the tablet having a hardness of 16.7 KP

which is deemed to be desirable for coating.

When the uncoated tablets shown in Table III were subjected to film coating, a tablet having a hardness of 5 KP indicated a remarkable weight loss on its surface at the beginning stage of the coating step thereby producing a significantly rough surface of the coated tablet. On the other hand, the tablet having a hardness of 16.7 KP produced the coated tablet having a smooth surface.

I declare further that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

Dated this 25 th day of March, 2003

By: Katsuya Matsuda
Katsuya Matsuda